



**NTP**  
National Toxicology Program

# Research Concept: 2',2'''-Dithiobisbenzanilide

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NTP Board of Scientific Counselors Meeting

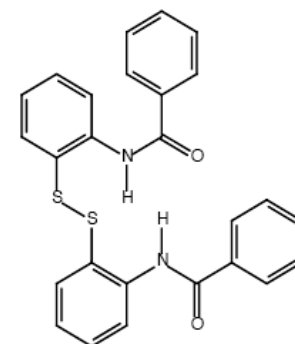
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## 2',2'''-Dithiobisbenzanilide (DTBBA)

- Nominated by the NCI based on:
  - High production volume
  - Lack of adequate toxicity data
  - Chemical structure
- Primarily used as a masticating agent and plasticizer in rubber production
  - Greatest use in the tire industry
  - U.S. production 1-10 million lbs/year 1998 and 2002
- Human exposure potential
  - Rubber industry workers - inhalation and dermal routes
  - General population - DTBBA or degradation products present in the environment and in consumer products
  - No specific exposure data
- Toxicological data
  - Low acute toxicity by oral and dermal routes
  - Skin sensitizer in guinea pigs
  - No genotoxicity, repeat dose toxicity or ADME studies





## Data Gaps and Key Issues

- Strong suspicion of toxicity based on chemical structure
- Little or no data describing the extent of exposure or the potential toxicity to humans
  - No subchronic or chronic toxicity studies in animals
  - Bioavailability, mutagenicity, and the potential for metabolic activation have not been determined
- Speculated that DTBBA is converted to biologically active benzanilide and N-phenyl benzamide derivatives *in vivo* and/or the environment
- Reactivity and/or potential skin metabolism of DTBBA is indicated by positive skin sensitization studies
- Mutagenicity studies of potential metabolites or degradation products may be warranted



## Proposed Research Program

- Determine the *in vitro* mutagenic potential of DTBBA
  - Data from these studies may be useful for characterizing the potential to form reactive metabolites
- Determine the potential for absorption of DTBBA through human and/or rodent skin *in vitro*
- Conduct *in vitro* metabolism studies using unlabeled DTBBA in human and/or rodent liver preparations
- Determine bioavailability and characterize metabolism of radiolabeled DTBBA in rodents



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## Questions and Comments